

U.S. SERIAL NO: 08/126,505
FILED: September 24, 1993
AMENDMENT

John E4 word.
Sequence ID No. 3); 12-16, 18-21: R-P-T-N-L...D-E-F-E (amino acids 12-21 of Sequence ID No. 1); 27,29: Y...N (amino acids 27, 29 of Sequence ID No. 1); 35, 64-65, 94: G...R-N...Y (amino acid 35 of Sequence ID No. 1, amino acids 4-5, 34 of Sequence ID No. 3), substitutions with structurally similar amino acids, and combinations thereof.

Remarks

Double Patenting Issues

The Examiner's careful review of the claims is greatly appreciated. They are indeed difficult to review. The specific embodiments which were identically claimed in the now issued parent application, U.S. Patent No. 5,545,619 have been deleted; a Terminal Disclaimer is enclosed in view of the partial overlap of some of the other embodiments in the claims.


Rejections under 35 U.S.C. §112

Claims 8, 9, 23 and 24 have been amended as suggested by the Examiner. Claims 1 and 16 have also been amended in a similar manner.

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Allowance of all pending claims 1, 3-5, 10-16, 18-20, 25-32, and 34, as amended, is earnestly solicited. A copy of all claims as amended upon entry of this amendment is enclosed for the convenience of the Examiner.

Respectfully submitted,

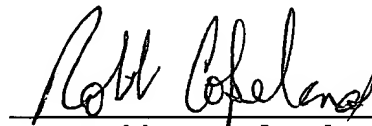

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CERTIFICATE OF MAILING UNDER 37 CFR §1.8a

I hereby certify that this paper, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner of Patents, Washington, D.C. 20231.

Date: December 13, 1996



Robb Copeland

Appendix: Claims as pending after entry of amendment

1. (four times amended) An analog of a protein [regulating complement activation having short consensus repeats of amino acid sequence] selected from the group of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and those complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein said protein analog is selected from the group consisting of complement regulating protein analogs containing short consensus repeats derived from a second, different complement regulating protein, complement regulating protein analogs wherein the short consensus repeats are rearranged, and complement regulating protein analogs consisting of as few as three short consensus repeats, wherein the protein analog binds C3b, C4b or C3b and C4b.

3. (amended) The analog of claim 1 wherein the protein is complement receptor one.

4. (amended) The analog of claim 1 wherein the protein is decay accelerating factor.

5. (amended) The analog of claim 1 wherein the protein is factor H.

8. (four times amended) An analog of a protein [regulating complement activation having short consensus repeats of amino acid sequence] selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and [those] these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains [a change within a] amino acid substitutions in the short consensus [repeat that corresponds] repeats which correspond [with a change to] to amino acid substitutions in the short consensus repeats of complement receptor one [as shown in Sequence] (SEQ ID No[.]: 13) selected from the group consisting of:

CR1-4 with its first 122 amino acids (SCR1-2) (Sequence ID Nos 1 and 3) replaced with CR1 amino acids 497-618 (SCR 8-9) (Sequence ID Nos. 2 and 4) and CR1-4(8,9) with deletion of 194-253; and substitution of amino acids 271-543 with: T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-P-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-P-P-H-V-K (Sequence ID No. 11), or structurally similar amino acids.

9. (five times amended) An analog of a protein [regulating complement activation having short consensus repeats of amino acid sequence] selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating

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factor, membrane cofactor protein, C4 binding protein, and factor H, and [those] these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains [a change within a] amino acid substitutions in the short consensus [repeat that corresponds] repeats which correspond [with a change to] to amino acid substitutions in the short consensus repeats of complement receptor one [as shown in Sequence] (SEQ ID No[.]: 13) selected from the group consisting of:

79: D (amino acid 19 of Sequence ID No. 4); 37,79: Y,D (amino acid 37 of Sequence ID No. 2 and amino acid 19 of Sequence ID No. 4); 92: T (amino acid 32 of Sequence ID No. 4); [109-112: N-A-A-H (amino acids 49-52 of Sequence ID No. 4); 109-112, 114-117, 121: N-A-A-H, S-T-K-P...Q (amino acids 49-52, 54-57, 61 of Sequence ID No. 4); 114-117, 121: S-T-K-P...Q; (amino acids 54-61 of Sequence ID No. 4) 116: K (amino acid 56 of Sequence ID No. 4); 116,117: K-P (amino acids 56-57 of Sequence ID No. 4);] 92-94: K...Y (amino acids 32-34 of Sequence ID NO. 3); 99,103,106: S...T...I (amino acids 39, 43 and 46 of Sequence ID No. 3); 109-112: D-T-V-I (amino acids 49-52 of Sequence ID No. 3); 110: T (amino acid 50 of Sequence ID No. 3); 111: V (amino acid 51 of Sequence ID No. 3); 112: I (amino acid 52 of Sequence ID No. 3); [114: D (amino acid 54 of Sequence ID No. 3); 115: N (amino acid 55 of Sequence ID No. 3); 121: D (amino acid 61 of Sequence ID No. 3); 117: T (amino acid 57 of Sequence ID No. 3);] 1,3: Q...N (amino acids 1, 3 of Sequence ID No. 1); 6-9: E-W-L-P (amino acids 6-9 of Sequence ID No. 1); 12-16, 18-21: K-L-K-T-Q...N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 27,29: S...K (amino acids 27,29 of Sequence ID No. 2); 37: S (amino acid 37 of Sequence ID No. 1); 44, 47, 49: I...K...S (amino acids 44, 47, 49 of Sequence ID No. 1); 52-54, 57, 59: T-G-A...R...R (amino acids 52-54, 57, 59 of Sequence ID No. 1); 78-79, 82: K-G...F (amino acids 18-19, 22 of Sequence ID No. 3); 85, 87: Q...K (amino acids 25, 27 of Sequence ID No. 3); 12-16, 18-21: R-P-T-N-L...D-E-F-E (amino acids 12-21 of Sequence ID No. 1); 27,29: Y...N (amino acids 27, 29 of Sequence ID No. 1); 35, 64-65, 94: G...R-N...Y (amino acid 35 of Sequence ID No. 1, amino acids 4-5, 34 of Sequence ID No. 3), substitutions with structurally similar amino acids, and combinations thereof.

10. (three times amended) An analog of decay accelerating factor wherein one or more substitutions are introduced into the region of the protein corresponding to decay accelerating factor short consensus repeats SCRs 2-3 as shown in Sequence ID No. 17 selected from the group consisting of 180-187: S-T-K-P-P-I-C-Q (amino acids 54-61 of Sequence ID No. 4); 175-178: N-A-A-H (amino acids 49-52 of Sequence ID No. 4); 175-187: S-T-K-P-P-I-C-Q-N-A-A-H (Sequence ID No. 9); 130: R (amino acid 4

of Sequence ID No. 3); 145: D (amino acid 19 of Sequence ID No. 4); 77-84: K-L-K-T-Q-T-N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 90-92: S-L-K (amino acids 27-29 of Sequence ID No. 2), substitutions with structurally similar amino acids, and combinations thereof.

11. The analog of claim 1 wherein the complement regulatory protein is factor H comprising sequences conferring on the protein an activity selected from the group consisting of C3b binding activity, C3b cofactor activity, C4b binding activity, and C4b cofactor activity, wherein the sequences are derived from a protein selected from the group consisting of complement receptor 1, membrane cofactor protein, C4 binding protein, and factor H.

12. The analog of claim 1 comprising at least one short consensus repeat derived from a different protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H.

13. (amended) The analog of claim 1 wherein the protein has C3b cofactor activity, C4b cofactor activity and decay accelerating activity.

14. (amended) The analog of claim 1 wherein the region of the protein having biological activity consists of three short consensus regions and has two complement regulatory activities.

15. The analog of claim 1 further comprising a pharmaceutically acceptable carrier for administration to a patient in need thereof.

16. (three times amended) A method for making an analog of a protein [regulating complement activation having short consensus repeats of amino acid sequence] selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, comprising

constructing a DNA sequence encoding a protein analog selected from the group consisting of complement regulating protein analogs containing short consensus repeats derived from a second, different complement regulating protein, complement regulating protein analogs wherein the short consensus repeats are rearranged, and complement regulating protein analogs consisting of as few as three short consensus repeats, wherein the protein analog binds C3b, C4b, or C3b and C4b, and

expressing the DNA sequence in a suitable host for expression of the protein.

18. The method of claim 16 wherein the protein is complement receptor one.

19. The method of claim 16 wherein the protein is decay accelerating factor.

20. The method of claim 16 wherein the protein is factor H.

23. (four times amended) A method for making a protein [regulating complement activation having short consensus repeats of amino acid sequence] selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and [those] these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains [a change within a] amino acid substitutions in the short consensus [repeat that corresponds] repeats which correspond [with a change to] to amino acid substitutions in the short consensus repeats of complement receptor one [as shown in Sequence] (SEQ ID No[.]: 13) selected from the group consisting of:

CR1-4 with its first 122 amino acids (SCR1-2) (Sequence ID Nos. 1 and 3) replaced with CR1 amino acids 497-618 (SCR 8-9) (Sequence ID Nos. 2 and 4) and CR1-4(8,9) with deletion of 194-253; substitution of amino acids 271-543 with: T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-P-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-P-P-H-V-K (Sequence ID No. 11), or structurally similar amino acids.

24. (four times amended) A method for making a protein [regulating complement activation having short consensus repeats of amino acid sequence] selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and [those] these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein the protein analog contains [a change within a] amino acid substitutions in the short consensus [repeat that corresponds] repeats which correspond [with a change to] to amino acid substitutions in the short consensus repeats of complement receptor one [as shown in Sequence] (SEQ ID No[.]: 13) selected from the group consisting of:

79: D (amino acid 19 of Sequence ID No. 4); 37,79: Y,D (amino acid 37 of Sequence ID No. 2 and amino acid 19 of Sequence ID No. 4); 92: T (amino acid 32 of Sequence ID No. 4); [109-112: N-A-A-H (amino acids 49-52 of Sequence ID No. 4); 109-112, 114-117, 121: N-A-A-H, S-T-K-P...Q (amino acids 49-52, 54-57, 61 of Sequence ID No. 4); 114-117, 121: S-T-K-P...Q; (amino acids 54-61 of Sequence ID No. 4) 116: K (amino acid 56 of Sequence ID No. 4); 116,117: K-P (amino acids 56-57 of Sequence ID No. 4);] 92-94: K...Y (amino acids 32-34 of Sequence ID NO. 3); 99,103,106: S...T...I

(amino acids 39, 43 and 46 of Sequence ID No. 3); 109-112: D-T-V-I (amino acids 49-52 of Sequence ID No. 3); 110: T (amino acid 50 of Sequence ID No. 3); 111: V (amino acid 51 of Sequence ID No. 3); 112: I (amino acid 52 of Sequence ID No. 3); [114: D (amino acid 54 of Sequence ID No. 3); 115: N (amino acid 55 of Sequence ID No. 3); 121: D (amino acid 61 of Sequence ID No. 3); 117: T (amino acid 57 of Sequence ID No. 3);] 1,3: Q...N (amino acids 1, 3 of Sequence ID No. 1); 6-9: E-W-L-P (amino acids 6-9 of Sequence ID No. 1); 12-16, 18-21: K-L-K-T-Q...N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 27,29: S...K (amino acids 27,29 of Sequence ID No. 2); 37: S (amino acid 37 of Sequence ID No. 1); 44, 47, 49: I...K...S (amino acids 44, 47, 49 of Sequence ID No. 1); 52-54, 57, 59: T-G-A...R...R (amino acids 52-54, 57, 59 of Sequence ID No. 1); 78-79, 82: K-G...F (amino acids 18-19, 22 of Sequence ID No. 3); 85, 87: Q...K (amino acids 25, 27 of Sequence ID No. 3); 12-16, 18-21: R-P-T-N-L...D-E-F-E (amino acids 12-21 of Sequence ID No. 1); 27,29: Y...N (amino acids 27, 29 of Sequence ID No. 1); 35, 64-65, 94: G...R-N...Y (amino acid 35 of Sequence ID No. 1, amino acids 4-5, 34 of Sequence ID No. 3), substitutions with structurally similar amino acids, and combinations thereof.

25. (three times amended) A method for making an analog of decay accelerating factor wherein one or more substitutions are introduced into the region of the protein corresponding to decay accelerating factor short consensus repeats SCRs 2-3 as shown in Sequence ID No. 17 selected from the group consisting of

180-187: S-T-K-P-P-I-C-Q (amino acids 54-61 of Sequence ID No. 4); 175-178: N-A-A-H (amino acids 49-52 of Sequence ID No. 4); 175-187: S-T-K-P-P-I-C-Q-N-A-A-H (Sequence ID No. 9); 130: R (amino acid 4 of Sequence ID No. 3); 145: D (amino acid 19 of Sequence ID No. 4); 77-84: K-L-K-T-Q-T-N-A-S-D (amino acids 12-21 of Sequence ID No. 2); 90-92: S-L-K (amino acids 27-29 of Sequence ID No. 2), substitutions with structurally similar amino acids, and combinations thereof.

27. (amended) The method of claim 16 comprising inserting into the protein analog at least one short consensus repeat derived from a different protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H.

34. (twice amended) A method for enhancing the C4b or C3b cofactor activity of a complement regulatory protein, wherein the protein has either C3b or C4b cofactor activity, comprising adding sequences to the protein conferring binding of the other ligand, either C4b or C3b, wherein the sequences are present in a protein selected from the group of naturally occurring complement

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receptor 1, complement receptor 2, decay accelerating factor,
membrane cofactor protein, C4 binding protein, and factor H.